

AMENDMENTS TO THE CLAIMS:

The listing of claims will replace all prior versions and listings of claims in the application:

1. (Previously Presented) A method for *in vivo* delivery of a fusion protein into the central nervous system (CNS), comprising administering to a human or an animal a fusion protein having a first protein comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) recombinantly fused to a second protein, wherein the non-toxic, proteolytic fragment of tetanus toxin comprises a fragment C and at least the 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C, and wherein said fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport in the CNS of the human or animal.
2. (Previously Presented) The method according to claim 1, wherein the fusion protein is administered into a muscle.
3. (Previously Presented) The method according to claim 2, wherein the fusion protein is administered into a muscle in the vicinity of a neuromuscular junction.
4. (Previously Presented) The method according to claim 2, wherein the muscle is selected in relation with the desired area of the CNS or spinal cord.
5. (Previously Presented) The method according to claim 1, wherein the fusion protein is administered into neuronal cells.
- 6-7. (Canceled)
8. (Previously Presented) The method according to claim 1, wherein the second protein is selected from the group consisting of protein SMN, BDNF (Brain-derived neurotrophic factor), NT-3 (Neurotrophin-3), NT-4/5, GDNF (Glial cell-line-

derived neurotrophic factor), IGF (Insulin-like growth factor), PNI (protease nexin I), SPI3 (Serine Protease Inhibitor protein), ICE (Interleukin-1 β converting enzyme), Bcl-2, GFP (green fluorescent protein), an endonuclease, an antibody, or a drug specifically directed against neurodegenerative diseases.

9. (Previously Presented) The method according to claim 8, wherein the composition comprises a combination of at least two of said second proteins.

10. (Previously Presented) The method according to claim 8, wherein the second protein is located upstream from the fragment of tetanus toxin.

11. (Previously Presented) The method according to claim 8, wherein the second protein is located downstream from the fragment of tetanus toxin.

12-30. (Canceled)

31. (Previously Presented) A method for treating a central nervous system (CNS) disease comprising:

administering to a patient in need thereof a composition comprising a fusion protein, wherein the fusion protein comprises a first protein comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) recombinantly fused to a second protein, wherein the non-toxic, proteolytic fragment of tetanus toxin comprises a fragment C and at least the 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C, and wherein the fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport when administered to the patient, wherein the fusion protein effectively treats said patient.

32. (Canceled)

33. (Previously Presented) The method according to claim 8, wherein the neurodegenerative disease is latero spinal amyotrophy (LSA).

34. (Previously Presented) The method according to claim 31, wherein the central nervous system disease is a neurodegenerative disease or a motoneuron disease.

35. (Previously Presented) The method according to claim 34, wherein the neurodegenerative disease or the motoneuron disease is amyotrophy lateral sclerosis, spinal muscular atrophy, or a neurodegenerative lysosomal storage disease.

36. (Previously Presented) The method according to claim 1 or 31, wherein the fusion protein comprises an amino acid sequence comprising SEQ ID NO:16.

37. (Previously Presented) The method according to claim 1 or 31, wherein the non-toxic, proteolytic fragment of tetanus toxin consists of a fragment C and the 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C.

38. (New) A method for *in vivo* delivery of a fusion protein into the central nervous system (CNS), comprising injecting into tongue or muscle of a human or an animal a fusion protein having a first protein comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) recombinantly fused to a second protein, wherein the non-toxic, proteolytic fragment of tetanus toxin comprises a fragment C and at least the 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C, and wherein said fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport in the brain stem or brain of the CNS of the human or animal.

39. (New) The method according to claim 38, which comprises injecting the fusion protein into the tongue of the human or animal, and the fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport in the brain of the CNS of the human or animal.

40. (New) The method according to claim 38, which comprises injecting the fusion protein into the muscle of the human or animal, and the fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport in the brain of the CNS of the human or animal.

41. (New) The method according to claim 38, which comprises injecting the fusion protein into the tongue of the human or animal, and the fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport in the brain stem of the CNS of the human or animal.

42. (New) The method according to claim 38, which comprises injecting the fusion protein into the muscle of the human or animal, and the fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport in the brain stem of the CNS of the human or animal.

43. (New) A method for *in vivo* delivery of a fusion protein into the central nervous system (CNS), comprising administering to a human or an animal a fusion protein having a first protein comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) recombinantly fused to a second protein,

wherein the non-toxic, proteolytic fragment of tetanus toxin comprises a fragment C and at least the 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C,

wherein the fragment of tetanus toxin is fused downstream of the second protein,
and

wherein said fusion protein undergoes *in vivo* retrograde axonal transport and
transsynaptic transport in the CNS of the human or animal.

44. (New) A method for treating a central nervous system (CNS) disease
comprising:

administering to a patient in need thereof a composition comprising a fusion
protein, wherein the fusion protein comprises a first protein comprising a non-toxic,
proteolytic fragment of tetanus toxin (TT) recombinantly fused to a second protein,

wherein the non-toxic, proteolytic fragment of tetanus toxin comprises a fragment
C and at least the 11 amino acid residues of fragment B that immediately precede the
amino terminus of fragment C,

wherein the fragment of tetanus toxin is fused downstream of the second protein,
and

wherein the fusion protein undergoes *in vivo* retrograde axonal transport and
transsynaptic transport when administered to the patient, wherein the fusion protein
effectively treats said patient.

45. (New) A method for *in vivo* delivery of a fusion protein into the central
nervous system (CNS), comprising administering to a human or an animal a fusion
protein having a first protein comprising a non-toxic, proteolytic fragment of tetanus
toxin (TT) recombinantly fused to a second protein,

wherein the non-toxic, proteolytic fragment of tetanus toxin consists of a fragment C and 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C (amino acids 854-1315 of the tetanus toxin holotoxin),

wherein said fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport in the CNS of the human or animal.

46. (New) A method for treating a central nervous system (CNS) disease comprising:

administering to a patient in need thereof a composition comprising a fusion protein, wherein the fusion protein comprises a first protein comprising a non-toxic, proteolytic fragment of tetanus toxin (TT) recombinantly fused to a second protein,

wherein the non-toxic, proteolytic fragment of tetanus toxin consists of a fragment C and 11 amino acid residues of fragment B that immediately precede the amino terminus of fragment C (amino acids 854-1315 of the tetanus toxin holotoxin),

wherein the fusion protein undergoes *in vivo* retrograde axonal transport and transsynaptic transport when administered to the patient, wherein the fusion protein effectively treats said patient.